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Rhodamine B Ingestion as a Cause of Fluorescent Red Urine

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RHODAMINE B is a compound with various commercial uses, most notably as a dye. Due to their toxic and carcinogenic potential,¹⁻⁴ rhodamine derivatives are not utilized as food additives and their use in cosmetics is restricted by the Food and Drug Administration (FDA). Two cases of rhodamine B ingestion were encountered at the University of California, San Diego (UCSD), Medical Center. Rhodamine B was found in food products allegedly purchased from a bakery in Tijuana, Mexico, and ingestion resulted in urine that fluoresced intensely under long-wave ultraviolet light. A report of human ingestion of rhodamine B has not been previously published.

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Reports of Cases

Case 1

The patient, a 17-year-old man, arrived at UCSD Medical Center complaining of red urine and left flank pain. He stated that he had been "kneed" in wrestling practice earlier that day. He said he had had no previous episodes of colored urine and did not use any drugs. On abdominal examination there were no abnormalities except for mild tenderness over the left iliac crest. The urine was bright red on examination. Both hematuria and myoglobinuria were excluded by laboratory analysis. Further questioning revealed that he had ingested large amounts of red chili peppers and cranberry juice 24 hours earlier. However, the patient had ingested this food combination on numerous occasions without having red urine. A urine specimen was then sent to the Toxicology Laboratory, UCSD Medical Center, for further analysis. There a series of intensely fluorescent compounds was detected by chromatography of the urine. On further investigation we learned that the patient had purchased "pink-colored" cookies from a bakery in Tijuana, Mexico, and had eaten several of them the previous day. The patient's family subsequently provided a cookie for analysis.

Case 2

A 25-year-old woman in her third trimester of pregnancy was admitted to UCSD Medical Center for evaluation of a recent seizure episode. Analysis of a specimen of her urine by the Toxicology Laboratory showed intensely fluorescent compounds. The patient said that she had visited Tijuana earlier in the week and had purchased numerous bakery goods there. However, she could not recall whether any of the goods were pink or red.

Laboratory Analysis

In the Toxicology Laboratory the urine specimens and the cookie showed intense red fluorescence under long-wave ultraviolet light. Thin-layer chromatography for drugs of abuse⁵ was done on the urine specimens from case 1 and case 2 and on a methanolic extract of the cookie from case 1. Five fluorescent compounds were noted in each of the urine specimens. Analysis of the cookie extract showed two fluorescent compounds, one of which corresponded to a major compound in the urine using five chromatography systems. Both infrared and ultraviolet-visible spectra for purified commercial rhodamine B and for one of the two compounds found in the cookie were identical. The amount of rhodamine B in the cookie was estimated gravimetrically to be at least 100 mg. Another major compound in the urine had ultraviolet and visible spectra identical to those published for triethylrhodamine, a rhodamine B metabolite.^{6,7} The other fluorescent compounds in the urine were conceivably further de-ethylated metabolites of rhodamine B,^{4,8} while the other compound in the cookie was either a contaminant or a degradation product of rhodamine.

Discussion

Rhodamine B ("basic violet 10," "food red 15," "FD&C red 19") is used commercially as a dye, fluorescent paint, analytic reagent and a cosmetic coloring agent.⁹ The compound has toxic properties and is considered to be a possible carcinogen.⁹ Oral administration to mice and rats is

ABBREVIATIONS USED IN TEXT

FDA = Food and Drug Administration

UCSD = University of California, San Diego

reported to cause lymphomas, stomach polyps, growth retardation and death due to hepatic damage.^{1,2,4} The compound also has shown mutagenic activity in the Ames test and it causes DNA damage in hamster ovary cells.³ The use of rhodamine B as a cosmetic additive in the United States is restricted by the FDA. Lipstick cannot contain more than 6% rhodamine B by weight and oral ingestion is limited to 0.75 mg per day.⁹ The cookie from case 1 contained more than 130 times this maximum allowed amount. While red urine due to dye or food ingestion is often considered innocuous, the two cases presented here suggest otherwise. The use of food additives in some countries is not as stringently controlled as in the United States.

In neither of the two cases, however, was there any direct evidence to suggest that the symptoms—case 1, flank pain; case 2, seizure—were associated with rhodamine B ingestion. Comparing symptoms with those of previous cases is not possible as this is the first report of human ingestion of rhodamine B. We do not know how widespread is the ingestion of rhodamine B, but the cookies can be easily obtained from bakeries in Tijuana. As to why rhodamine B was used to color

bakery goods, one can only speculate. The most likely explanation is its brilliant pink to red color and its fluorescent properties.

Addendum

Since preparation of this manuscript, additional cookies containing rhodamine B were obtained from a store in Tijuana. Apparently this is a continuing problem.

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Treatment of Chronic Myelomonocytic Leukemia

Vincristine and Prednisone Therapy During Symptomatic Phase or After Transformation to Acute Leukemia

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PRIMARY DISORDERS of bone marrow production characterized by varying dysplastic abnormalities have been termed myelodysplastic syndromes. Included among these are refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation and chronic myelomonocytic leukemia.^{1,2} Treatment of patients with these disorders has been unsatisfactory, particularly after transformation to a symptomatic phase of disease with or without transformation to acute leukemia. We report here four cases of patients with chronic myelomonocytic leukemia who were symptomatic or whose disorders had changed to acute leukemia and who

achieved hematologic remissions after receiving vincristine sulfate and prednisone.

Methods

Peripheral blood and bone marrow smears were stained with Wright-Giemsa stain according to standard techniques. Histochemical stains were done as previously described.³ Terminal deoxynucleotidyl transferase (TdT)-positive blood cells were detected using rabbit anti-bovine TdT (Bethesda Research Laboratories, Gaithersburg, Md),⁴ and fluorescence developed with fluorescein-conjugated, goat anti-rabbit immunoglobulin G. Both positive and negative controls were run with each specimen.

Patient Characteristics and Results of Treatment

The characteristics of four patients seen with chronic myelomonocytic leukemia at the University of California, San Diego (UCSD), Medical Center are summarized in Table 1. All four patients had elevated leukocyte counts and more than 1,000 circulating monocytes per μ l. Bone marrows in all patients showed myeloid hyperplasia with varying numbers of monocytes and monocyte precursors. Three patients had palpable spleens. Other supporting laboratory data varied. Patient 1 had bone marrow karyotypic analysis done on three separate occasions, showing only normal metaphases. She underwent marrow transformation to acute leukemia, and histochemical stains were compatible with acute myelomonocytic leukemia. Patient 2 presented with systemic symptoms including fevers, sweats, weight loss and peripheral edema. His serum lactic dehydrogenase (LDH) level was greatly elevated (Table 1), but the peripheral blood differential showed only small numbers of circulating blast cells. Patient 3 also had a transformation of his condition to acute leukemia. Blast

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